REMARKS

Claims 1-13 and 17-19 are pending. The Applicant respectfully (a) amend the claims herewith with to distinguish the prior art and address the Examiner's concerns with 35 USC §112, paragraph 1.

35 USC §102. The Examiner alleges that the subject matter of claims 1-19 is anticipated by Haigh, *et al.*, WO 9413650 as well as by the cited publication by Buckle, *et al.*

The Applicants herewith amend claims 1-3, 5-6, 8, 13, and 17 to distinguish the prior art. Particularly, X is now defined as O in formula I. The Applicants accordingly respectfully request the Examiner to withdraw the rejection.

Rejections under 35 USC §112, pargraph 1

As suggested by the Examiner, the Applicants amend the scope of the compounds within the subject matter of the claims 1-19 now presented to address the Examiners concern as to enablement. Particularly, Ring A, fused to ring B, represents a 6 membered cyclic ring, which may contain one nitrogen atom and may optionally be substituted with one or more alkyl; the ring A may be saturated or aromatic;

Ring B, fused to ring A, is a benzene ring;

X and Y are independently O;

Z represents O, or NR^6 wherein R^6 represents hydrogen or alkyl;

Q represents O, or NR^7 wherein R^7 represents hydrogen or alkyl;

R^1, R^2 and R^3 are independently H or alkyl;

R^4, R^5 are independently H or alkyl;

Ar is benzene.

The Applicants moreover limit the method of use claims to a method of treatment (claim 13) and wherein the condition is selected from type 2 diabetes, dyslipidemia, and obesity (claim 17).

The Applicants accordingly respectfully request the Examiner to withdraw the rejection.

Written Description

The subject matter of each of claims 13 and 17-19 of the pending application is alleged by the Examiner to lack support by the disclosure under the statutory requirement for written description.

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.[1] The PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.

The Federal courts have consistently reversed rejections asserting a lack of description for inventions claiming a pharmacological or therapeutic utility where an applicant has provided evidence that reasonably supports such a use.

The Applicants respectfully point out to the Examiner that *in vivo* data is not necessary to satisfy the statutory requirement for written description of the use a compound to treat a disease condition when that disease condition relates to an art-accepted biological model and that model is used to illustrate the expected efficacy of the class of compounds.

A REASONABLE CORRELATION BETWEEN THE EVIDENCE AND THE ASSERTED USE IS SUFFICIENT

As a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating

[1] See, e.g., Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. Nelson v. Bowler, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

DATA FROM IN VITRO OR ANIMAL TESTING IS GENERALLY SUFFICIENT

Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish an invention related to treatment of human disorders (see In re Isaacs, 347 F.2d 889, 146 USPQ 193 (CCPA 1963); In re Langer, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974)), even with respect to situations where no art-recognized animal models existed for the human disease encompassed by the claims. Ex parte Balzarini, 21 USPQ2d 1892 (Bd. Pat. App. & Inter. 1991) (human clinical data is not required to demonstrate the utility of the claimed invention.

A well-established and routine art-accepted protocol to evaluate a candidate agent's agonistic activity of PPAR is by means of a cell-based reporter gene assay. Particularly, activation of PPAR in cell-based reporter gene assays is an art-accepted model that corresponds very closely to efficacy of the agent *in vivo*. The Applicants indeed employed such a technology (reporter gene assay) and, in doing so, unambiguously exemplified species representative of the invention, *see* Figures 1, 2, 5, 6, 7, 8, 9, and 10, for example. The representative species are illustrated to exhibit agonistic activity of PPAR with characteristics of distinct activation profile over PPARγ, or PPARγ and PPARα, or PPARα, γ, and δ.[2] Representative species are further tested, as disclosed, in relevant animal model of *db/db*, a well-established and commonly known transgenic model which mimics late stage pathological changes in human type 2 diabetes. Efficacy is illustrated in treating various disease conditions as exemplified in Figures 3 and 4.

In summary, one skilled in the art, in view of the state of the art - *and* - the facts of the Applicants' Specification, can easily recognize the disclosure and identification of agonist compounds of the present invention as well as their art-expected use in preventing, controlling, and treating type 2 diabetes, dyslipidimia, and obeisity, for example.

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[2] Reflected by the fold activation over the basal level and comparing to positive control such as Ros for PPARγ, Wy for PPARα, and 2-Bro for PPARδ.

Modulation of the biological activity of these receptors is indeed widely-accepted in clinic practice and is well-documented in many preclinical and clinical studies for controlling and treating associated disease conditions including but not limited to human type 2 diabetes and dyslipidemia. The PPARγagonists Rosiglitazone and Piglitazone, for example, are well-known for treating human type 2 diabetes. PPARα agonists Fenofibrate and Clofibrate, for example, are well-documented for treating human dyslipidemia.

As stated *supra*, the Applicants unambiguously exemplified species representative of the invention, *see* Figures 1, 2, 5, 6, 7, 8, 9, and 10, for example, illustrated to exhibit agonistic activity of PPAR with characteristics of distinct activation profile over PPARγ, or PPARγ and PPARα, or PPARα, γ, and δ.

The Applicants respectfully request the Examiner to withdraw all rejections under 35 USC §112, pargraph 1.

For the foregoing reasons, the Applicant submits that Claims 1-13 and 17-19 are in condition for allowance. Early action toward this end is courteously solicited.

The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No.02-4800.

Respectfully submitted,

Patrick H. Higgins
Attorney for the Applicants
Registration No. 39,709

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Buchanan Ingersoll & Rooney PC
P.O. Box 1404, Alexandria
VA 22313-1404
(609) 987-6811 (voice)